REMARKS

Claims 1, 3, 4, 6, 8-17 and 20-22 are pending in the application. Claims 6, 8-17 and 20-22 are withdrawn. Applicants note that the Examiner in the Office Action dated March 22, 2007 indicates that claims 20 and 21 were added in the Amendment filed on December 14, 2006. However, claim 22 was added also. Applicants respectfully request that the Examiner indicate that claim 22 was added and is pending but withdrawn since it is dependent on withdrawn claim 15.

1. Claims Withdrawn From Consideration As Belonging To Non-Elected Groups Should Be Considered

Claims 6, 8-17, 20, 21 and 22 are withdrawn from consideration by the Examiner as belonging to a non-elected group. These claims incorporate all the limitations recited in the product claims. Since Applicants believe that the product claims are allowable, claims 6, 8-17, 20, 21 and 22 should be considered by the Examiner. Applicants respectfully request that these claims be considered by the Examiner.

2. The Rejection of Claims 1, 3, and 4 Under 35 U.S.C. § 103(a), Should Be Withdrawn

Claims 1, 3, and 4 are rejected under 35 U.S.C. § 103(a) as being, allegedly, unpatentable over Taylor *et al.*, J. Immunol. 1992. 148(8): 2462-2468 ("Taylor") in view of Kimberly *et al.*, J. Clin. Invest. 1989. 84(3): 962-970 ("Kimberly") and Emlen *et al.*, J. Immunol. Meth. 1990. 132(1): 91-101 ("Emlen"). Applicants respectfully disagree with the Examiner for the reasons set forth below.

A finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and the content of the prior art, the differences between the invention and the prior art, the level of the ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and whether one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be successful. *In re O'Farrell*, 853 F.2d 894, 902-4 (Fed. Cir. 1988); *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Both the suggestion of the claimed invention and the expectation of success must be in the prior art, not in the disclosure of the claimed invention. *In re Dow*

Chemical Co., 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In determining obviousness, "the inquiry is not whether each element existed in prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed." *Hartness Int'l Inc. v. Simplimatic Eng'g Co.*, 819 F.2d 1100, 2 U.S.P.Q.2d 1826 (Fed. Cir. 1987). An analysis under 35 U.S.C. § 103(a) "should be made explicit," and "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1736 (2007), WL 1237834, at *14 and *15, respectively (2007).

The presently claimed invention relates to an antigen-based heteropolymer (AHP) comprising (a) a monoclonal antibody that specifically binds a complement receptor (CR1) site on a primate erythrocyte, and (b) an antigen specific for a target pathogenic antibody or autoantibody, in which the monoclonal antibody is crosslinked to the antigen. The AHP, when administered to a human or non-human primate, facilitates binding of the target pathogenic antibody or autoantibody to erythrocytes and subsequent clearance of the target pathogenic antibody or autoantibody from the circulation of the human or non-human primate. The presently claimed invention also relates to erythrocytes franked with the AHP and to methods for treating or detecting an autoimmune disease using the AHP.

Taylor, however, teaches a bispecific heteropolymer comprising a first mAb that binds a CR1 receptor on a primate erythrocyte and a second mAb that binds the DNP-bovine γ-globulin (DNP-BGG) (see Taylor Abstract). Taylor teaches that injection in squirrel monkeys of DNP-BGG followed by the heteropolymer leads to E binding and clearance from the circulation of a significant fraction of both the heteropolymers and the DNP-BGG (see Taylor Abstract). Taylor suggests that the method can be used to treat diseases associated with blood-borne pathogens (see Taylor Abstract). Taylor also showed that partial heteropolymers lacking the second mAb were not cleared (see, *e.g.*, Taylor at page 2467, right column, 4th paragraph). Taylor suggests that the "mechanism of clearance may involve recognition of Fc regions of IgG not directly associated with CR1", *i.e.*, of the non-anti-CR1 IgG (see, *e.g.*, Taylor at page 2467, right column, 4th paragraph). In contrast to the present invention, Taylor does not teach or suggest an antigen-based heteropolymers (AHP) comprising an anti-CR1 antibody crosslinked to an antigen that is recognized by a pathogenic antibody or autoantibody. Nor does Taylor teach or suggest that such an AHP can be used to clear pathogenic antibody or autoantibody.

Kimberly discloses a study of *in vivo* handling of soluble complement fixing Ab/dsDNA immune complexes in chimpanzees. Kimberly teaches that C-fixing antibody/dsDNA immune complexes bound efficiently to erythrocytes of chimpanzees (see Kimberly Abstract). The chimpanzee erythrocyte-bound IC can be stripped from the erythrocyte rapidly by the mononuclear phagocyte system without sequestration of the erythrocyte (see Kimberly Abstract). Kimberly does not concern heteropolymers or antigen-based heteropolymers. Thus, although Kimberly teaches antibody/dsDNA immune complexes can be cleared by an IC-mediated process, Kimberly does not teach or suggest that an AHP can be used to clear a pathogenic antibody or autoantibody.

Emlen teaches an ELISA assay for the detection of antibodies that bind double-stranded DNA. Emlen teaches biotinylating dsDNA such that they can be bound to streptavidin coated wells (see Emlen Abstract). The well-bound DNAs remained double stranded, and did not lose their antigenicity to their antibodies (see Emlen Abstract). Emlen does not concern heteropolymers or antigen-based heteropolymers. Nor does Emlen relate to clearance of antibodies/dsDNA complexes in the circulation of a primate. Emlen merely teaches what has been known in the prior art that antibodies bind to antigens and has no bearing on the presently claimed invention.

Applicants submit that Taylor, Kimberly, or Emlen, alone or in combination, neither provide to a person skilled in the art a suggestion nor a reasonable expectation of success to modify Taylor's bispecific heteropolymer to create the AHP of the present invention. Applicants submit that Taylor does not teach or suggest modifying its bispecific heteropolymer by replacing the second mAb in its bispecific heteropolymer with an antigen so as to create an AHP and that on the contrary, Taylor teaches that the Fc regions of the second antibody are required for clearance. Taylor teaches that the HP containing only anti-CR1 mAb and Sa are not cleared after E binding because clearance requires the presence of the Fc regions of a second antibody, *i.e.*, the Fc regions a non-anti-CR1 IgG. Thus, Taylor not only does not teach or suggest modifying its bispecific heteropolymer by replacing the second mAb with an antigen, but also teaches against making such a modification as it would render the resulting product unsuitable for its intended purpose, *i.e.*, clearance of pathogens.

With regard to the Examiner's contention that he has been unable to find, and Applicants have not pointed out where in Taylor it is taught that the presence of the Fc portion of the second antibody is required for clearance, Applicants invite the Examiner's attention to Taylor at page 2467, right column, 4th paragraph, which states:

> In the experiments with rhesus monkeys (Fig. 4), it is intriguing that after E binding the complete HP are cleared (with and without associated Ag), yet the 'partial' HP containing only anti-CR1 mAb and SA) are not cleared after E binding. This suggests the mechanism of clearance may involve recognition of Fc regions of IgG not directly associated with CR1.

The relevant inquiry for a finding of obviousness is whether the prior art suggests the invention, and whether one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be successful. *In re O'Farrell*, 853 F.2d 894, 902-4 (Fed. Cir. 1988); *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Taylor clearly neither suggests the claimed invention, nor does it provide the skilled artisan with a reasonable expectation the claimed invention would be successful. On the contrary, based on Taylor, one of ordinary skill in the art would have had a reasonable expectation that the claimed invention would be **unsuccessful**.

As discussed previously, neither Kimberly or Emlen supplies what is missing in Taylor. As discussed above, although Kimberly teaches antibody/dsDNA immune complexes can be cleared by an IC-mediated process, Kimberly does not teach or suggest that an AHP can be used to clear a pathogenic antibody or autoantibody. Although Emlen teaches biotinylating dsDNA such that it can be bound to streptavidin coated wells and retain its antigenicity, Emlen does not relate to heteropolymers or antigen-based heteropolymers, much less clearance of antibodies/dsDNA complexes in the circulation of a primate using such heteropolymers or antigen-based heteropolymers. Thus, neither Kimberly or Emlen teaches or suggests modifying Taylor's bispecific heteropolymer to generate the AHP of the present invention. In addition, neither Kimberly or Emlen suggest to a person skilled in the art that the Fc regions of the second antibody are not required for clearance, and, thus, that an AHP, which lacks such Fc regions, would be able to achieve the purpose of clearance of pathogens. Thus, neither Kimberly or Emlen provide teachings to a person skilled in the art that would overcome the discouragement provided by Taylor. As such, neither Taylor, Kimberly, or Emlen, alone or in combination, provide to a person skilled in the art the suggestion and the reasonable expectation of success to modify Taylor's bispecific heteropolymer to create the AHP of the present invention.

In view of the foregoing, Applicants respectfully submit that claims 1, 3 and 4 are not rendered obvious under 35 U.S.C. § 103(a) by Taylor in view of Kimberly and Emlen, and that the rejection of these claims under 35 U.S.C. § 103(a) based on Taylor in view of

Kimberly and Emlen should be withdrawn. For the same reasons, withdrawn claims 6, 8-17 and 20-22 are also novel and nonobvious over the cited references.

CONCLUSION

Applicants respectfully request that the above-made amendments and remarks of the present response be entered and made of record in the file history of the present application. Applicants submit that the presently pending claims meet all requirements for patentability and respectfully request allowance and action for issuance.

Applicants request that the Examiner call the undersigned at (212) 326-3939 if any questions or issues remain.

Respectfully submitted,

Date: October 31, 2007

Laura A. Coruzzi — 30,742
Laura A. Coruzzi (Reg. No.)

By: William J. Thomann — 40,203
William J. Thomann (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 326-3939